Fatal adenovirus 32 infection in a bone marrow transplant recipient

A K Charles, E O Caul, H J Porter, A Oakhill

Abstract

A case of disseminated adenovirus type 32 infection causing severe hepatitis, gastrointestinal ulceration and also with respiratory involvement is reported in a bone marrow transplant recipient. Typical viral inclusions were seen in the postmortem histological sections and adenovirus infection was confirmed using in situ hybridisation and isolation of adenovirus type 32 from separate organs at necropsy. This is the first case in which adenovirus type 32 was the cause of fatal disseminated disease in a bone marrow transplant recipient.


Keywords: Adenovirus, bone marrow transplant, in situ hybridisation.
transplant when eight months old and was treated with the immunosuppressive agents cyclosporin A and Campath. After transplant-plantation, the patient had an episode of diarrhoea, when adenovirus was cultured from the faeces, and several episodes of febrile neutropenia including Staphylococcus aureus and haemolytic streptococcal bacteraemias. Six days before he died, the patient developed an ileus, which was managed conservatively. Gram positive cocci were cultured from blood. Four days later the patient developed respiratory distress and required ventilation. He deteriorated with refractory hypotension and died.

**Postmortem findings**

At necropsy, the lungs were firm, heavy and oedematous with petechial haemorrhages. There were ulcers in the ileum, the liver was flabby and yellow, and there was mild ascites. The bones were solid and there was increased cerebrospinal fluid in the subarachnoid space around the brain. The remaining organs were macroscopically normal. Histologically, the lungs showed changes consistent with adult type respiratory distress syndrome, with hyaline membranes, intra-alveolar macrophages and organising exudate. The larynx was ulcerated and occasional “brick-like” intranuclear inclusions were seen in the squamous epithelium and adjacent glands (fig 1).

In the liver there was extensive necrosis involving both perportal and centrilobular areas. Many hepatocytes contained eosinophilic intranuclear inclusions. The ileum showed mucosal ulceration, some villous atrophy, and intranuclear inclusions were seen in the superficial epithelium and in adjacent crypts which showed regenerative changes. Inclusions were also occasionally present in stromal cells in the submucosa deep within the ulceration. Similar inclusions were seen in the appendix. The inclusions seen in the larynx, liver and bowel were typical of those described in adenovirus infections.

Focal ischaemic changes were seen in the myocardium. The bones showed histological changes consistent with osteopetrosis. Little bone marrow engraftment was seen.

**In situ hybridisation**

A biotinylated DNA probe for adenovirus (Enzo Diagnostics, New York, USA) was hybridised to the postmortem, paraffin wax embedded tissues, using standard techniques. Hybridised probe was detected using Streptavidin complexed with alkaline phosphatase, with NBT-BCIP as the chromogen (Kreatech Biotin detection system). The slides were counterstained with neutral red. An appendix with adenovirus inclusions served as a positive control.

The probe produced a reactive product in all cells showing intranuclear inclusions on light microscopy, as well as in some adjacent epithelial cells in hepatocytes (fig 2), trachea and bowel. The stromal cells with intranuclear in-

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**Case report**

The patient was a male infant in whom infantile osteopetrosis was diagnosed at the age of four months with evidence of hydrocephalus and optic atrophy. He received a bone marrow engraftment, tubulointerstitial nephritis and haemorrhagic cystitis, and a case of meningocencephalitis.

In situ hybridisation permits the identification of specific viruses in the tissue sections and has been used for detecting adenovirus infection. This technique was used to confirm the nature of the intranuclear viral inclusions seen with routine histological stains.
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A C Bateman, P J Gallagher, A C Vincenti

Abstract

Spontaneous dissection of the coronary arteries is an uncommon condition that may lead to sudden, fatal coronary artery occlusion. Three cases of sudden death attributable to coronary artery occlusion are presented. Dissection was associated with Marfan’s syndrome in the first case, and occurred three weeks postpartum in the second case. In case 1, dissection occurred within the intima, and was not associated with an inflammatory cell infiltrate. In cases 2 and 3, dissection occurred between the tunica media and the external elastic lamina, and was associated with a mixed inflammatory infiltrate, rich in eosinophils, T lymphocytes, and histiocytes. The spatial limitation of the inflammatory infiltrate to the adventitial compartment, together with the absence of inflammation in case 1, suggests a reactive origin rather than a causative role for the inflammatory cells. Detailed examination of serial blocks of any coronary artery occlusion is essential in young patients.

Sudden death from coronary artery dissection

A C Bateman, P J Gallagher, A C Vincenti

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